Response to the December 19, 2002 Office Action

Amendments to the Specification:

Please replace the paragraph beginning at pg. 6, line 16, with the following amended paragraph:

The term "complements of a polynucleotide molecule" denotes a polynucleotide molecule having a complementary base sequence and reverse orientation as compared to a reference sequence.

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Please replace the paragraph beginning at pg. 6, line 20, with the following amended paragraph:

The term "contig" denotes a polynucleotide that has a contiguous stretch of identical or complementary sequence to another polynucleotide. Contiguous sequences are said to "overlap" a given stretch of polynucleotide sequence either in their entirety or along a partial stretch of the polynucleotide.

Please replace the paragraph beginning at pg. 10, line 7, with the following amended paragraph:

Processing of the protein involves cleavage at the C-terminus of the signal peptide, and, based on predicted structural homology with other mature members of the insulin family, a cleavage at the C-terminus of the B chain and at the N-terminus of the A chain, resulting in removal of the C-peptide. Analysis of the zins4 polypeptide of SEQ ID NO:2 with other known members of the insulin family suggests a signal peptide cleavage site in the region of amino acid residue 25 (Ala) of SEQ ID NO:2. Cleavage at the C-terminus of the B chain is predicted to be at the C-terminal of amino acid residue 53 (Arg) or residue 54 (Arg) followed by cleavage of the Arg residues by carboxypeptidase to leave amino acid residue 52 (Trp) as the C-terminal amino acid residue. Cleavage sites resulting in the N-terminus of the A chain are suggested in the region of amino acid residue 115 (Arg) to 118 (Arg). Cleavage is predicted to be after the C-terminus of amino acid residue 118 (Arg) leaving amino acid residue 119 (Asp) as the N-terminal amino acid residue of the A chain. The C-terminal amino acid is residue 142 (Cys). The cleavage site at the

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junction of the C-peptide and A chain is highly conserved, occurring after Arg-X-X-Arg (SEQ ID NO:13; wherein X is any amino acid residue), Arg-Arg or Lys-Arg; however, the cleavage sites at the junction of the signal sequence and B chain, and at the junction of the B chain and C-peptide, do not maintain a similarly high degree of conservation within the insulin family.